Supporting Information: Palladium Catalyzed Coupling of Vinylogous Amides With Aryl Halides: Applications to the Synthesis of Heterocycles

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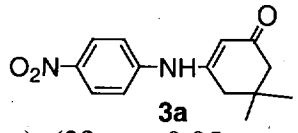
General Methods: All reactions were carried out using Radley's Carousel Reaction Station under a positive pressure of dry nitrogen. Reactions were stirred using Teflon coated magnetic stir bars. Tetrahydrofuran (THF), enaminone **1**, cesium carbonate, $Pd_2(dba)_3$, and the aryl halides were purchased from Aldrich and used without further purification. Although ligand **4** was synthesized in four steps using published procedures, **4** is currently commercially available from Strem Chemical Co. along with the other ligand 2-(dicyclohexylphosphino)biphenyl which was tolerated under the described conditions. All crude products were isolated and purified by preparative thin layer chromatography using Analtech 1500 or 1000 micron plates and ethyl acetate and hexanes purchased from Fisher. ^1H and ^{13}C NMR spectra were recorded on Varian instruments at 500 and 125 MHz respectively. The IR spectrum was recorded with a Perkin-Elmer 1320 spectrometer and mass spectra were recorded using a low resolution Hewlett-Packard Series 1100 LC-MS.

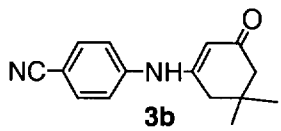
Experimental Procedures

Representative Procedure for 3. $Pd_2(dba)_3$ (23 mg, 0.05 mmol) was added to a mixture of bromide **2d** (128 mg, 0.75 mmol), enaminone **1** (70 mg, 0.5 mmol), ligand **4** (20 mg, 0.05 mmol), and Cs_2CO_3 (260 mg, 0.8 mmol), in 5 mL of THF. Next, the mixture was stirred at 80 °C under nitrogen until TLC showed complete reaction (24 h). The reaction mixture was then diluted with 120 mL of EtOAc, washed with saturated NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated. The crude orange oil was then purified by preparative TLC (SiO_2, 80% EtOAc/Hexanes) to afford **3d** (88 mg, 77%) as a waxy yellow solid.



3a

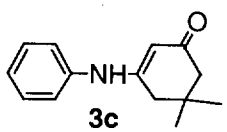
Optimal Procedure for 3a. $Pd_2(dba)_3$ (23 mg, 0.05 mmol) was added to a mixture of chloride **2j** (75 mg, 0.54 mmol), enaminone **1** (70 mg, 0.5 mmol), ligand **4** (20 mg, 0.05 mmol), and Cs_2CO_3 (185 mg, 0.6 mmol), in 5 mL of THF. Next, the mixture was stirred at 80 °C under nitrogen until TLC showed complete reaction (2.5 h). The reaction mixture was then diluted with 120 mL of EtOAc, washed with saturated NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated. The crude orange solid was then purified by preparative TLC (SiO_2, 80% EtOAc/Hexanes) to afford **3a** (130 mg, 92%) as a yellow-orange solid. ^1H NMR (500 MHz, $CDCl_3$) δ = 8.22 (d, J = 8.9 Hz, 1 H), 7.30 (d, J = 9.2 Hz, 1 H), 6.55 (br s, 1 H), 5.89 (s, 1 H), 2.42 (s, 2 H), 2.30 (s, 2 H), 1.15 (s, 6 H). ^{13}C NMR (125 MHz, DMSO) δ = 197.3, 158.2, 147.0, 142.3, 126.0 (2 C), 121.0 (2 C), 101.9, 50.8, 40.5, 32.9, 28.5 (2 C). LC-MS (M^++1) 261.0.



3b

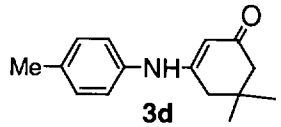
Data for Compound 3b. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.61 (d, J = 8.9 Hz, 1 H), 7.26 (d, J = 9.0 Hz, 1 H), 6.70 (br s, 1 H), 5.81 (s, 1 H), 2.40 (s, 2 H), 2.28 (s, 2 H), 1.13 (s, 6 H). ^{13}C NMR (125 MHz,

$CDCl_3$) δ = 199.0, 159.3, 143.6, 133.6 (2 C), 122.4 (2 C), 118.9, 107.1, 100.8, 50.6, 43.6, 33.0, 28.5 (2 C). LC-MS (M^++1) 241.2.



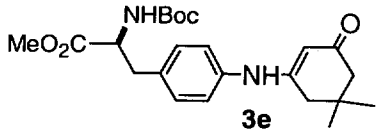
3c

Data for Compound 3c. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.63 (br s, 1 H), 7.26 (t, J = 7.9 Hz, 2 H), 7.13-7.11 (m, 3 H), 5.54 (s, 1 H), 2.35 (s, 2 H), 2.17 (s, 2 H), 1.05 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.3, 162.4, 138.8, 129.3 (2 C), 125.5, 124.1 (2 C), 97.6, 50.6, 43.3, 32.9, 28.5 (2 C). LC-MS (M^++1) 216.2.



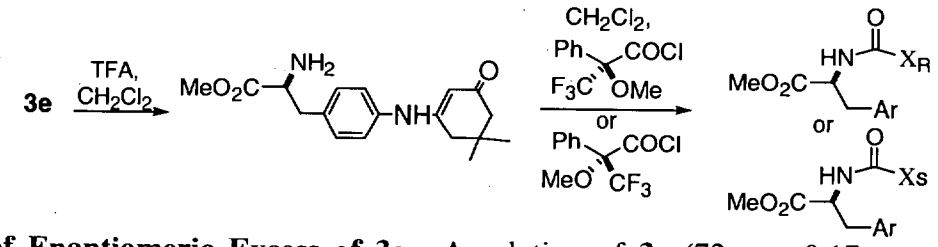
3d

Data for Compound 3d. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.22 (br s, 1 H), 7.09 (d, J = 8.3 Hz, 2 H), 7.01 (d, J = 8.2, 2 H), 5.49 (s, 1 H), 2.33 (s, 2 H), 2.18 (s, 2 H), 1.06 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.0, 161.9, 135.9, 135.5, 130.0 (2 C), 1, 124.3 (2 C), 98.0, 50.6, 43.5, 33.0, 28.5 (2 C). LC-MS (M^++1) 230.0.



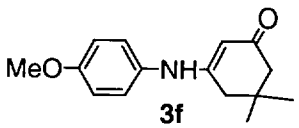
3e

Procedure for 3e. $Pd_2(dba)_3$ (23 mg, 0.05 mmol) was added to a mixture of bromide **2e** (70 mg, 0.195 mmol), enaminone **1** (25 mg, 0.18 mmol), ligand **4** (20 mg, 0.05 mmol), and Cs_2CO_3 (160 mg, 0.49 mmol), in 5 mL of THF. Next, the mixture was stirred at 80 °C under nitrogen until TLC showed complete reaction (20 h). The reaction mixture was then diluted with 100 mL of EtOAc, washed with saturated NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated. The crude oil was then purified by preparative TLC (SiO_2, 80% EtOAc/Hexanes) to afford **3e** (72 mg, 96%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.44 (br s, 1 H), 7.06 (d, J = 8.7 Hz, 2 H), 7.03 (d, J = 8.4 Hz, 2 H), 5.55 (s, 1 H), 5.07 (d, J = 7.8 Hz, 1 H), 4.53-4.49 (m, 1 H), 3.07-2.92 (m, 2 H), 2.33 (s, 2 H), 2.17 (s, 2 H), 1.39 (s, 9 H), 1.04 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.1, 172.4, 161.4, 155.4, 137.6, 133.3, 130.3 (2 C), 123.9 (2 C), 98.3, 80.2, 54.7, 52.5, 50.5, 43.5, 37.9, 33.0, 28.52 (2 C), 28.49 (3 C). LC-MS (M^++1) 417.3.



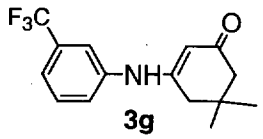
Analysis of Enantiomeric Excess of 3e. A solution of **3e** (72 mg, 0.17 mmol) in 10 mL of 1:1 TFA/CH_2Cl_2 was stirred at room temperature for 10 min then concentrated to give 52 mg (95%) of the resulting amine which was used without further purification. ^{1}H NMR (500 MHz, CD_3OD) δ = 7.23 (d, J = 8.2 Hz, 2 H), 7.16 (d, J = 8.4 Hz, 2 H), 5.46 (s, 1 H), 3.75 (t, J = 7.0 Hz, 1 H), 3.68 (s, 3 H), 3.02 (dd, J = 13.7, 6.2 Hz, 1 H), 2.94 (dd, J = 13.7, 6.9 Hz, 2 H), 2.45 (s, 2 H), 2.21 (s, 2 H), 1.11 (s, 6 H). ^{13}C NMR (125 MHz, CD_3OD) δ = 199.2, 174.6, 164.8, 137.4, 134.7, 130.2 (2 C), 124.1 (2 C), 96.1, 55.4, 51.3, 49.5, 42.4, 39.8, 32.5, 27.2 (2 C). LC-MS (M^++1) 217.2.

Next, the amine was divided into 2 equal portions which were stirred under nitrogen at room temperature with Mosher's acid chlorides (R and S, 27.4 mg, 0.086 mmol each) for 15 min at which time TLC showed complete reaction. The reaction mixtures were then concentrated and purified by preparative TLC (80% EtOAc/Hex) to afford each product. ^{1}H-NMR analysis of each product revealed that a 2:1 mixture (33% ee) of diastereomers was present in each case.



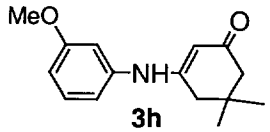
3f

Data for Compound 3f. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.07 (d, J = 8.9 Hz, 2 H), 6.85 (d, J = 9.0 Hz, 2 H), 6.59 (br s, 1 H), 5.38 (s, 1 H), 3.80 (s, 3 H), 2.33 (s, 2 H), 2.20 (s, 2 H), 1.10 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 197.7, 162.2, 157.9, 131.0, 126.5 (2 C), 114.7 (2 C), 98.0, 55.7, 50.5, 43.5, 33.1, 28.6 (2 C). LC-MS (M^++1) 246.0.



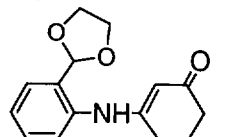
3g

Data for Compound 3g. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.16 (1 H), 7.38-7.31 (m, 4 H), 5.50 (s, 1 H), 2.38 (s, 2 H), 2.18 (s, 2 H), 1.04 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.3, 161.7, 139.5, 132.0, 130.0, 127.1, 123.8, 121.9, 120.5, 98.3, 50.6, 43.3, 32.9, 28.3 (2 C). LC-MS (M^++1) 284.1.



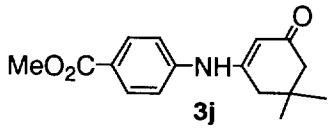
3h

Data for Compound 3h. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.67 (s, 1 H), 7.16 (t, J = 8.0 Hz, 1 H), 6.72-6.64 (m, 3 H), 5.58 (s, 1 H), 3.72 (s, 3 H), 2.33 (s, 2 H), 2.16 (s, 2 H), 1.04 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.3, 161.7, 160.5, 139.9, 130.1, 116.3, 111.0, 109.9, 98.4, 55.5, 50.6, 43.4, 32.9, 28.5. LC-MS (M^++1) 246.2.



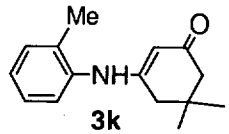
3i

Data for Compound 3i. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48 (dd, J = 8.0, 1.7 Hz, 1 H), 7.33-7.28 (m, 2 H), 7.14 (td, J = 7.8, 1.7 Hz, 1 H), 7.00 (br s, 1 H), 5.82 (s, 1 H), 5.51 (s, 1 H), 4.06-3.99 (m, 4 H), 2.32 (s, 2 H), 2.19 (s, 2 H), 1.08 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.1, 160.3, 137.1, 130.9, 129.8, 127.4, 125.5 (2 C), 102.0, 99.0, 65.3 (2 C), 50.5, 43.9, 33.1, 28.5 (2 C). LC-MS (M^++1) 288.1.



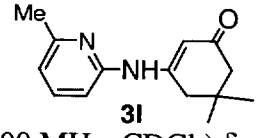
3j

Data for Compound 3j. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.95 (d, J = 8.7 Hz, 2 H), 7.36 (br s, 1 H), 7.20 (d, J = 8.7 Hz, 2 H), 5.77 (s, 1 H), 3.91 (s, 3 H), 2.39 (s, 2 H), 2.24 (s, 2 H), 1.09 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.7, 166.6, 159.4, 143.3, 131.2 (2 C), 126.1, 121.9 (2 C), 100.4, 52.3, 50.5, 43.8, 33.0, 28.5 (2 C). LC-MS (M^++1) 274.0.



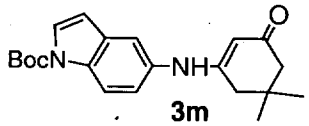
3k

Data for Compound 3k. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.45 (br s, 1 H), 7.18-7.10 (m, 3 H), 7.01 (dd, J = 8.5, 2.3 Hz, 1 H), 4.87 (s, 1 H), 2.32 (s, 2 H), 2.12 (s, 3 H), 2.09 (s, 2 H), 1.02 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 197.6, 163.7, 136.6, 134.8, 131.2, 127.41, 127.39, 127.0, 97.3, 50.5, 43.0, 33.1, 28.4 (2 C), 17.9. LC-MS (M^++1) 230.3.



3l

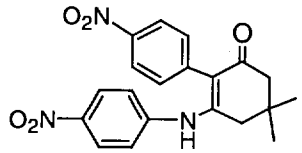
Data for Compound 3l. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.53 (t, J = 7.9 Hz, 1 H), 6.92 (d, J = 8.2 Hz, 1 H), 6.83 (d, J = 7.4 Hz, 1 H), 6.82 (br s, 1 H), 6.32 (s, 1 H), 2.47 (s, 3 H), 2.38 (s, 2 H), 2.26 (s, 2 H), 1.11 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.2, 158.1, 156.6, 152.0, 138.5, 118.4, 111.1, 102.9, 50.6, 44.4, 32.9, 28.5 (2 C), 24.4. LC-MS (M^++1) 231.3.



3m

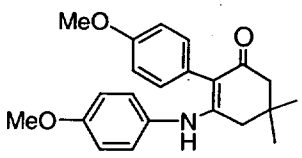
Procedure for 3m. Commercially available 6-bromoindole (1.0 g, 5.1 mmol), DMAP (1.5 g, 5.1 mmol) and Boc_2O (1.68 g, 8.0 mmol) in 20 mL of CH_2Cl_2 was stirred at room temperature for 60 min then the reaction mixture was concentrated and purified by Biotage aided flash chromatography to afford an excellent yield (1.34 g, 90%) of the protected indole **2p**.

$Pd_2(dba)_3$ (23 mg, 0.05 mmol) was added to a mixture of bromide **2p** (207 mg, 0.70 mmol), enaminone **1** (70 mg, 0.5 mmol), ligand **4** (20 mg, 0.05 mmol), and Cs_2CO_3 (170 mg, 0.6 mmol), in 5 mL of THF. Next, the mixture was stirred at 80 °C under nitrogen until TLC showed complete reaction (24 h). The reaction mixture was then diluted with 120 mL of EtOAc, washed with saturated NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated. The crude oil was then purified by preparative TLC (SiO_2, 80% EtOAc/Hexanes) to afford **3m** (115 mg, 65%). ^1H NMR (125 MHz, $CDCl_3$) δ = 8.03 (br d, J = 7.7 Hz, 1 H), 7.57 (s, 1 H), 7.31 (d, J = 1.9 Hz, 1 H), 7.05 (dd, J = 8.9, 2.1 Hz, 1 H), 6.44 (d, J = 3.6 Hz, 1 H), 5.50 (s, 1 H), 2.33 (s, 2 H), 2.15 (s, 2 H), 1.66 (s, 9 H), 1.03 (s, 6 H). ^{13}C NMR (500 MHz, $CDCl_3$) δ = 198.0, 162.7, 149.7, 133.4, 131.3, 127.1, 121.4, 116.8, 115.9, 107.3, 97.5, 84.2, 50.5, 43.4, 33.0, 28.5 (2 C), 28.4 (3 C). LC-MS (M^++1) 355.2.



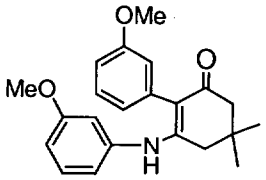
5a

Data for Compound 5a. ^1H NMR (500 MHz, $CDCl_3$) δ = 8.14 (d, J = 8.9 Hz, 2 H), 8.12 (d, J = 8.7 Hz, 2 H), 7.39 (d, J = 8.7 Hz, 2 H), 7.08 (d, J = 9.2 Hz, 2 H), 7.03 (s, 1 H), 2.65 (s, 2 H), 2.42 (s, 2 H), 1.18 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 194.7, 155.5, 146.9, 144.7, 144.0, 141.7, 132.5 (2 C), 125.3 (2 C), 124.1 (2 C), 122.8 (2 C), 116.2, 50.9, 41.6, 33.4, 28.4 (2 C). LC-MS (M^++1) 382.2.



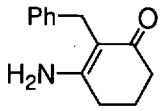
5f

Data for Compound 5f. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.19 (dd, J = 6.8, 2.2 Hz, 1 H), 6.98 (dd, J = 6.9, 2.1 Hz, 1 H), 6.95 (dd, J = 7.1, 1.9 Hz, 1 H), 6.86 (dd, J = 6.9, 2.1 Hz, 1 H), 6.38 (s, 1 H), 3.82 (s, 3 H), 3.81 (s, 3 H), 2.37 (s, 2 H), 2.35 (s, 2 H), 1.11 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 194.3, 159.0, 158.6, 158.1, 132.5 (2 C), 131.4, 127.6 (2 C), 126.5, 115.0 (2 C), 114.7 (2 C), 113.1, 55.7, 55.5, 51.0, 40.3, 32.7, 28.6 (2 C). LC-MS (M^++1) 352.2.



5h

Data for Compound 5h. ^1H NMR (500 MHz, $CDCl_3$) δ = 7.36 (t, J = 7.9 Hz, 1 H), 7.23 (t, J = 8.1 Hz, 1 H), 6.87-6.81 (m, 2 H), 6.81 (s, 1 H), 6.74 (dd, J = 8.3, 2.3 Hz, 1 H), 6.59 (d, J = 7.9 Hz, 1 H), 6.53-6.51 (m, 2 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 2.49 (s, 2 H), 2.39 (s, 2 H), 1.13 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 194.4, 160.5, 160.4, 157.3, 139.8, 135.9, 130.4, 130.2, 123.5, 117.5, 116.8, 114.5, 113.3, 111.3, 111.2, 55.6, 55.5, 51.0, 40.6, 33.0, 28.5 (2 C). LC-MS (M^++1) 353.2.

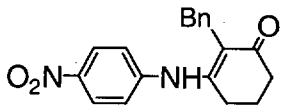


7

Procedure for Enaminone 7. β-diketone **6** (3.0g, 14.8 mmol) and ammonium acetate (2.31g, 30 mmol) were heated to reflux with a Dean-Stark trap in 100 mL of 5% AcOH/benzene until reaction was complete (3 h). After cooling to room temperature, the mixture was diluted with 400 mL of sat'd

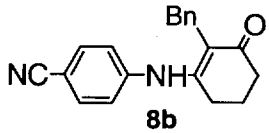
$NaHCO_3$, extracted with EtOAc/MeOH (10:1), the organic layers combined and washed with brine (2 x 50 mL), dried over $MgSO_4$, filtered and concentrated. The crude product **7** (2.5 g of a pale yellow crystalline solid, 86%) was pure by TLC and NMR and was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.21 (t, J = 8.2 Hz, 2 H), 7.14-7.12 (m, 3 H), 4.87 (br s, 2 H), 3.61 (s, 2 H), 2.38-2.34 (m, 4 H), 1.91 (quin, J = 6.3 Hz, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.8, 162.1, 140.6, 128.7 (2 C), 128.1 (2 C), 126.1, 108.9, 36.7, 29.7, 28.5, 21.6. LC-MS (M^++1) 201.9.

Representative Procedure for 8. $Pd_2(dba)_3$ (15 mg, 0.017 mmol) was added to a mixture of bromide **2f** (94 mg, 0.5 mmol), enaminone **7** (67 mg, 0.33 mmol), ligand **4** (13 mg, 0.05 mmol), and Cs_2CO_3 (163 mg, 0.75 mmol), in 5 ml of dry THF. Next, the mixture was stirred at 80 °C under nitrogen until TLC showed complete reaction (48 h). The reaction mixture was then diluted with 120ml of EtOAc and washed with saturated NH_4Cl (20 ml) and brine (20 ml), dried over Na_2SO_4, filtered and concentrated. The crude orange oil was then purified by preparative TLC (SiO_2, 70 % EtOAc/Hexanes) to afford **8f** (91 mg, 90 %) as a pale yellow solid.



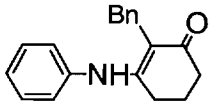
8a

Data for Compound 8a. ^{1}H NMR (500 MHz, Acetone-d6) δ = 8.15 (d, J = 8.9 Hz, 2 H), 8.04 (s, 1 H), 7.21-7.08 (m, 7 H), 3.79 (s, 2 H), 2.78 (t, J = 6.1 Hz, 2 H), 2.41 (t, J = 6.6, 2H), 2.05-1.97 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 196.6, 156.5, 145.5, 143.1, 139.5, 129.2 (2 C), 128.2 (2 C), 126.7, 125.4 (2 C), 121.2 (2 C), 116.9, 37.1, 29.0, 28.1, 22.7. LC-MS (M^++1) 261.0.



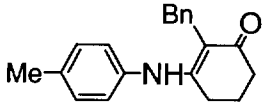
8b

Data for Compound 8b. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.49 (d, J =8.7 Hz, 2 H), 7.29-7.18 (m,5H), 6.83 (d, J = 8.7 Hz, 2 H), 6.79 (s, 1 H), 3.80 (s, 2 H), 2.60 (t, J = 6.0 Hz, 2 H), 2.47 (t, 6.4 Hz, 2 H), 2.15-1.98 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 196.4, 157.0, 143.5, 139.7, 133.5 (2 C), 129.1 (2 C), 128.2 (2 C), 126.7, 122.4 (2 C), 119.0, 115.8, 106.8, 37.1, 28.9, 27.8, 27.8, 22.6. LC-MS (M^++1) 303.1.



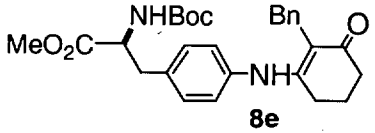
8c

Data for Compound 8c. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.32-7.14 (m, 8H), 6.84 (d, J = 7.8 Hz, 2 H), 6.48 (s, 1 H), 3.86 (s, 2 H), 2.51-2.47 (m, 4 H), 1.97-1.94 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.8, 159.7, 140.3, 138.8, 129.4 (2 C), 129.0 (2 C), 128.3 (2 C), 126.4, 125.7, 125.0 (2 C), 111.7, 37.0, 28.8, 27.3, 22.3. LC-MS (M^++1) 278.1.



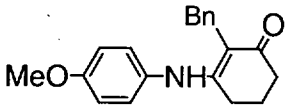
8d

Data for compound 8d. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.31-7.18 (m, 5 H), 7.08 (d, J = 8.0 Hz, 2 H), 6.76 (d, J = 8.2 Hz, 2 H), 6.43 (s, 1 H), 3.85 (s, 2 H), 2.48-2.44 (m, 4 H), 2.32 (s, 3 H), 1.97-1.93 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.6, 160.1, 140.4, 136.1, 135.8, 130.0 (2 C), 128.9 (2 C), 128.3 (2 C), 126.3, 125.3 (2 C), 111.1, 36.9, 28.7, 27.3, 22.2, 21.1. LC-MS (M^++1) 291.4.



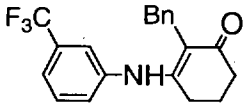
8e

Data for compound 8e. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.26-7.14 (m, 5 H), 7.02 (d, J = 8.2 Hz, 2 H), 6.73 (d, J = 8.4 Hz, 2 H), 6.47 (s, 1 H), 5.13 (d, J = 8.0 Hz, 1 H), 4.52-4.48 (m, 1 H), 3.80 (s, 2 H), 3.67 (s, 3 H), 3.08-3.04 (m, 1 H), 2.95-2.91 (m, 1 H), 2.45-2.41 (m, 4 H), 1.94-1.89 (m, 2 H), 1.38 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.7, 172.4, 159.7, 155.3, 140.3, 137.6, 133.8, 130.2 (2 C), 128.9 (2 C), 128.2 (2 C), 126.3, 125.0 (2 C), 111.6, 80.1, 54.7, 52.5, 37.9, 36.9, 28.6 (3 C), 28.5, 27.3, 22.2. LC-MS (M^++1-tButyl) 423.1.



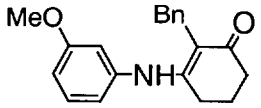
8f

Data for compound 8f. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.31-7.18 (m, 5 H), 6.81 (s, 4 H), 3.85 (s, 2 H), 3.79 (s, 3 H), 2.47 (t, J = 6.4 Hz, 2 H), 2.83 (t, J = 6.1 Hz, 2 H), 1.97-1.92 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.5, 160.7, 158.1, 140.5, 131.5, 128.8 (2 C), 128.3 (2 C), 127.4 (2 C), 126.2, 114.5 (2 C), 110.5, 55.7, 36.9, 28.6, 27.2, 22.1. LC-MS (M^++1) 308.2



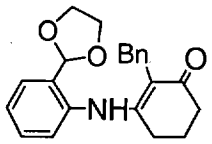
8g

Data for compound 8g. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.42-7.22 (m, 6 H), 7.06 (s, 1 H), 6.99 (d, J = 7.1 Hz, 1 H), 6.46 (s, 1 H), 3.86 (s, 2 H), 2.53-2.50 (m, 4 H), 2.04-2.99 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 196.1, 158.3, 139.9, 139.5, 130.0, 129.2 (2 C), 128.2 (2 C), 127.4, 126.6, 121.9, 120.9, 120.8, 113.4, 37.0, 28.8, 27.3, 22.3. LC-MS (M^++1) 346.2.



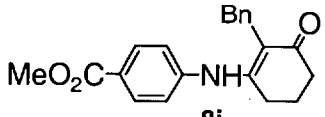
8h

Data for compound 8h. ^{1}H NMR (500 MHz, Acetone-d6) δ = 7.36 (s, 1 H), 7.27-7.20 (m, 4 H), 7.12 (t, J = 7.2 Hz, 1 H), 6.72 (dd, J = 2.5 Hz, 8.4 Hz, 1 H), 6.63-6.60 (m, 2 H), 3.82 (s, 2 H), 3.76 (s, 3 H), 2.62-2.59 (m, 2 H), 2.33 (t, J = 6.5 Hz, 2 H), 1.96-1.91 (m, 2 H). ^{13}C NMR (125 MHz, Acetone-d6) δ = 194.6, 160.5, 159.1, 141.5, 141.0, 129.9, 128.5 (2 C), 128.3 (2 C), 125.7, 117.3, 111.8, 110.8, 110.7, 55.1, 36.9, 28.1, 27.7, 22.4. LC-MS (M^++1) 308.2.



8i

Data for compound 8i. ^{1}H NMR (500 MHz, Acetone-d6) δ = 7.50 (dd, J = 1.6 Hz, 7.6 Hz, 1 H), 7.37 (td, J = 1.6 Hz, 7.8 Hz, 1 H), 7.28-7.12 (m, 7H), 5.52 (s, 1 H), 3.93-3.81, (m, 4 H), 2.52 (t, J = 6.4 Hz, 2 H), 2.35 (t, J = 6.6 Hz, 2 H), 1.96-1.91 (m, 2 H). ^{13}C NMR (125 MHz, Acetone-d6) δ = 194.3, 159.0, 140.9, 138.1, 132.5, 129.6, 128.4 (2 C), 128.3 (2 C), 127.2, 126.3, 125.8, 125.3, 111.8, 101.0, 65.2 (2 C), 36.9, 28.2, 27.4, 22.3. LC-MS (M^++1) 350.2.

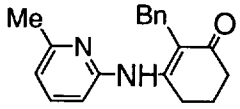


8j

Data for compound 8j. ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 7.91 (d, J = 8.5 Hz, 2 H), 7.29-7.17 (m, 5 H), 6.81 (d, J = 8.7 Hz, 2 H), 6.73 (s, 1 H), 3.86 (s, 3 H), 3.82 (s, 2 H). 2.59 (t, J = 6.1 Hz, 2 H), 2.47 (t, J = 6.6 Hz, 2 H), 2.02-1.96 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 196.2, 166.6, 157.9, 143.4, 139.9, 131.0 (2 C), 129.0 (2 C), 128.2 (2 C), 126.5, 125.8, 122.3 (2 C), 114.4, 52.3, 37.0, 28.8, 27.7, 22.6. LC-MS (M^++1) 336.1.

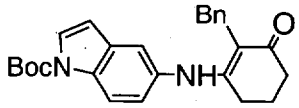
8k

Data for compound 8k. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.30-7.25 (m, 3 H), 7.20-7.10 (m, 4 H), 6.97 (d, J = 7.3 Hz, 1 H), 6.11 (s, 1 H), 3.88 (s, 2 H), 2.49 (t, J = 6.4 Hz, 2 H), 2.31 (t, J = 6.1 Hz, 2 H), 1.98-1.92 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.5, 160.6, 140.5, 137.3, 134.5, 131.1, 129.0 (2 C), 128.3 (2 C), 127.1, 126.9, 126.8, 126.4, 111.1, 36.9, 28.8, 27.1, 22.2, 17.5. LC-MS (M^++1) 292.1.



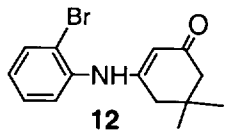
8l

Data for compound 8l. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.42 (t, J = 7.8 Hz, 1 H), 7.31-7.18 (m, 5 H), 6.85 (s, 1 H), 6.77 (d, J = 7.5 Hz, 1 H), 6.36 (d, J = 8.0 Hz, 1 H), 3.84 (s, 2 H), 2.99 (t, J = 6.2 Hz, 2 H), 2.52 (t, J = 6.7 Hz, 2 H), 2.44 (s, 3 H), 2.06-2.01 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 196.8, 157.8, 157.7, 152.2, 140.1, 138.3, 129.0 (2 C), 128.3 (2 C), 126.4, 117.3, 114.9, 111.2, 37.2, 29.0, 28.3, 24.5, 22.6. LC-MS (M^++1) 293.1.

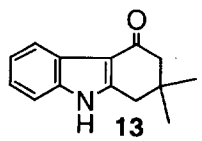


8m

Data for compound 8m. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.06 (d, J = 8.0 Hz, 1 H), 7.62 (d, J = 3.4 Hz, 1 H), 7.33-7.20 (m, 5 H), 7.07 (sd, J = 1.8 Hz, 1 H), 6.83, (dd, J = 2.0 Hz, J = 8.7 Hz, 1 H), 6.5 (s, 1 H), 6.49 (s, 1 H), 3.88 (s, 2 H), 2.50-2.43 (m, 4 H), 1.97-1.92 (m, 2 H), 1.68 (s, 9 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.6, 160.7, 149.7, 140.4, 133.5, 131.2, 128.9 (2 C), 128.3 (2 C), 127.5, 126.3, 122.6, 118.0, 115.8, 110.8, 107.1, 84.3, 36.9, 28.7, 28.4, 27.3, 22.2. LC-MS (M^++1) 417.2.

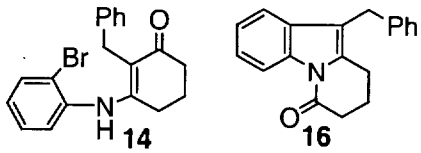


12



13

Procedure for the Formation of 13. $Pd_2(dba)_3$ (23 mg, 0.05 mmol) was added to a mixture of dibromide **11** (180 μL, 1.0 mmol), enaminone **1** (70 mg, 0.5 mmol), ligand **4** (20 mg, 0.05 mmol), and Cs_2CO_3 (423 mg, 1.3 mmol), in 5 mL of THF. Next, the mixture was stirred at 80 °C under nitrogen until TLC showed complete disappearance of **1** (12 h) and the appearance of a mixture of **12** and **13**. The reaction mixture was then cooled to room temperature at which time an additional portion of $Pd_2(dba)_3$ (23 mg, 0.05 mmol) and ligand **4** (20 mg, 0.05 mmol) was added and the reaction mixture was heated to reflux for an additional 24 h. The reaction mixture was then diluted with 120 mL of EtOAc, washed with saturated NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated. The crude oil was then purified by preparative TLC (SiO_2, 40% EtOAc/Hexanes) to afford **13** (65 mg, 61%). For **12**, ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.59 (dd, J = 7.1, 0.9 Hz, 1 H), 7.35 (d, J = 7.8 Hz, 1 H), 7.28 (t, J = 7.2 Hz, 1 H), 7.05 (dt, J = 8.7, 1.0 Hz, 1 H), 6.41 (br s, 1 H), 5.40 (s, 1 H), 2.39 (s, 2 H), 2.22 (s, 2 H), 1.11 (s, 6 H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 198.3, 160.1, 136.9, 133.5, 128.4, 127.3, 126.6, 119.2, 99.6, 50.6, 43.6, 33.1, 28.5 (2 C). Enaminone **12** and indole **13** have been reported in the literature (reference 15a in the communication). This reported synthesis of **13** was accomplished in 2 steps and less than 9% yield via condensation of dimedone with 2-bromoaniline followed by intramolecular Heck cyclization.



Procedure for the Formation of 14 and 16. $Pd_2(dba)_3$ (23 mg, 0.05 mmol) was added to a mixture of dibromide **11** (180 μL, 1.0 mmol), enaminone **1** (101 mg, 0.5 mmol), ligand **4** (20 mg, 0.05 mmol), and Cs_2CO_3 (423 mg, 1.3 mmol), in 5 mL of THF. Next, the mixture was stirred at 80 °C under nitrogen until TLC showed complete disappearance of **1** (12 h) and the appearance of a mixture of **14** and **16**. The reaction mixture was then cooled to room temperature at which time an additional portion of $Pd_2(dba)_3$ (23 mg, 0.05 mmol) and ligand **4** (20 mg, 0.05 mmol) was added and the reaction mixture was heated to reflux for an additional 24 h. The reaction mixture was then diluted with 120 mL of EtOAc, washed with saturated NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated. The crude oil was then purified by preparative TLC (SiO_2, 40% EtOAc/Hexanes) to afford **16** (116 mg, 84%). For **14**, ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.53 (dd, J = 8.0, 1.4 Hz, 1 H), 7.32-7.16 (m, 6 H), 7.07 (dd, J = 8.0, 1.1 Hz, 1 H), 7.02 (dt, J = 7.8, 1.3 Hz, 1 H), 6.41 (br s, 1 H), 3.88 (s, 2 H), 2.52 (t, J = 6.4 Hz, 2 H), 2.47 (t, J = 6.2 Hz, 2 H), 2.01 (quin, J = 6.3 Hz, 2 H); LC-MS (M^++1) 358.1. For **16**, IR ($CDCl_3$) 3068, 3026, 2954, 2910, 2839, 1703, 1617, 1494, 1458 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.54 (d, J = 7.9 Hz, 1 H), 7.40 (d, J = 7.9 Hz, 1 H), 7.34-7.22 (m, 7 H), 4.06 (s, 2 H), 2.94 (t, J =6.3 Hz, 2 H), 2.81 (t, J = 6.3 Hz, 2 H), 2.11 (quin, J = 6.3 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.5, 140.0, 135.0, 134.7, 130.6, 128.8 (2C), 128.5 (2C), 126.5, 124.5, 124.1, 118.6, 116.7, 115.6, 34.7, 30.2, 22.2, 21.5; LC-MS (M^++1) 276.19.